NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

INDUSTRIAL TECHNOLOGY RESEARCH INSTITUTE,
Appellant

v.

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,
Appellee

2015-1200

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board, in Interference No. 105,970.

Decided: January 29, 2016

ERIK R. PUKNYS, Finnegan, Henderson, Farabow, Garrett & Dunner, LLP, Palo Alto, CA, argued for appellant. Also represented by MICHAEL PAUL BARKER.

EDWARD R. REINES, Weil, Gotshal & Manges LLP, Redwood Shores, CA, argued for appellee. Also represented by MICHELE GAUGER, DEREK C. WALTER.

Before PROST, *Chief Judge*, LOURIE and WALLACH, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Industrial Technology Research Institute and Ti-Shiue Biotech, Inc. (collectively, "ITRI") appeal from the decision of the United States Patent and Trademark Office Patent Trial and Appeal Board ("Board") awarding judgment to Pacific Biosciences of California, Inc. ("PacBio") in Interference No. 105,970. *Indus. Tech. Research Inst. v. Pac. Biosciences of Cal., Inc.*, Interference No. 105,970, 2014 WL 4381078, at *1 (P.T.A.B. Sept. 3, 2014) ("*Board Decision*"). The Board terminated the interference after it determined that all of ITRI's involved claims, *viz.*, claims 1–28 of U.S. Patent 8,486,630 ("the '630 patent"), would have been obvious over the cited prior art, and that PacBio, the senior party, was entitled to the benefit of the filing date of its U.S. Provisional Application 61/201,551 ("the '551 application") because that application adequately described an embodiment of the interference Count. *Id.* at *31. For the reasons that follow, we *affirm in part*, *vacate in part*, and *remand* for further proceedings consistent with this opinion.

BACKGROUND

I

The technology at issue relates to methods of detecting modified bases in nucleic acids. Deoxyribonucleic acid ("DNA") is a polymeric molecule having repeating units of nucleotide bases—adenine ("A"), guanine ("G"), cytosine ("C"), and thymine ("T")—that are covalently linked together via a sugar-phosphate backbone. DNA carries genetic information in the sequence of those bases. DNA also carries epigenetic information when one or more bases are chemically modified. For example, C at a given position in the DNA sequence may be naturally methylated and instead exist as 5-methylcytosine ("^{m}C"). Such

DNA methylation plays an important role in the regulation of gene expression. '630 patent col. 2 ll. 14–15. Detecting modified bases in the DNA sequence would facilitate the further study of their epigenetic effects.

DNA usually exists in a double-stranded form, with two strands coiled around each other in a double helix. The two strands are often referred to as the "forward" and "reverse" strands. In the double helix, each base on one strand pairs with a base on the other strand according to the Watson-Crick base pairing rules—A pairs with T, and C with G. Thus, the forward and reverse strands typically have complementary sequences.

A DNA sequence may be determined using sequencing-by-synthesis ("SBS") methods. During DNA synthesis, a parent strand is separated from its complement, and an enzyme catalyzes the synthesis of a new complementary strand by adding nucleotides, one at a time, to that new strand, using the parent strand as a template and pairing bases according to the Watson-Crick rules. The SBS technique monitors the order of nucleotide addition to the growing new strand, and from that deduces the sequence of the complementary template strand.

Traditional SBS methods might not readily distinguish a base from its modified form. For example, C and ^{m}C would both pair with G during SBS. Detecting the addition of a G to the growing new strand only suggests that either C or ^{m}C is at the corresponding position of the template strand. According to ITRI, some prior-art methods relied on bisulfite conversion to distinguish C from ^{m}C. Appellant's Br. 2, 10–11. Thus, one first obtains a reference sequence of the DNA being studied. A sample of that DNA is then treated with bisulfite, which converts C to uracil ("U"), but does not affect ^{m}C or other bases. The bisulfite-treated DNA is then sequenced. Because U pairs preferentially with A, not G, comparing the bisulfite-treated DNA sequence with the untreated reference

sequence would reveal the positions of the C-to-U conversion, whereas the ^{m}C positions would show no change, thus distinguishing C from ^{m}C in the DNA sequence.

II

ITRI owns the '630 patent, which claims a method of determining the position of at least one modified base in a double-stranded nucleic acid. Claim 24 is representative and reads as follows:[1]

> 24. A method of determining a sequence of a double-stranded nucleic acid sample and a position of at least one modified base in the sequence, comprising:
>
> a. locking the forward and reverse strands of the nucleic acid sample together to form a circular pair-locked molecule;
>
> b. obtaining sequence data of the circular pair-locked molecule via single molecule sequencing, wherein sequence data comprises sequences of the forward and reverse strands of the circular pair-locked molecule; and
>
> c. *determining the sequence of the double stranded nucleic acid sample and the position of the at least one modified base in the sequence of the double stranded nucleic acid sample by comparing the sequences of the forward and reverse strands of the circular pair-locked molecule, wherein at least one modified base in the double-stranded nucleic sample is paired with a*

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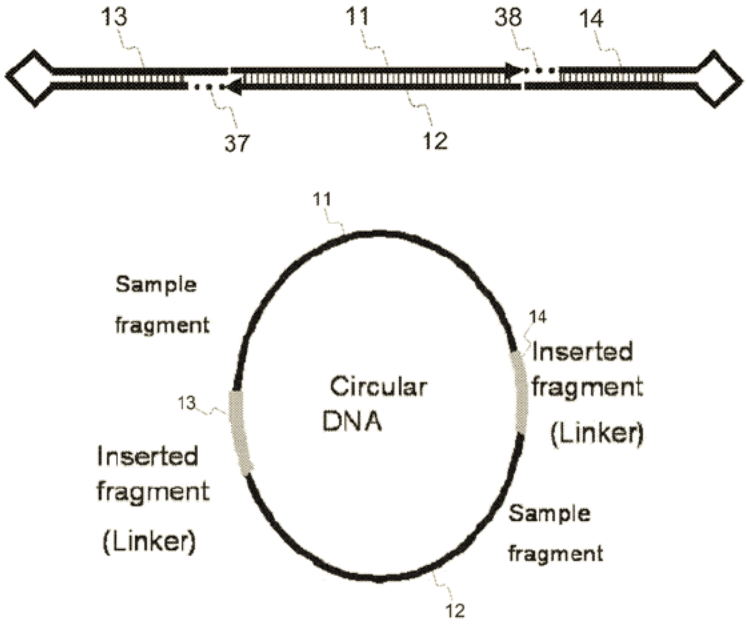
[1] As indicated *infra*, the sole count of the interference is identical to claim 24 of the '630 patent.

> *base having a base pairing specificity different from its preferred partner base.*

'630 patent col. 47 ll. 31–49 (emphasis added).

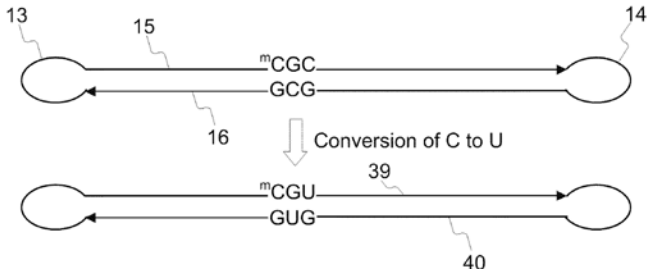
Claim 24 thus requires three steps. First, a double-stranded nucleic acid is converted to a circular pair-locked molecule ("CPLM") by linking the forward and reverse strands at their ends. The '630 patent illustrates a CPLM in Figures 3A and 3B; both are reproduced below.



Id. figs.3A & 3B.

Then, the CPLM is sequenced. Because the CPLM is a circular DNA that contains what were previously separate, but complementary, forward and reverse strands, the CPLM sequence includes the sequences of the forward and reverse strands. Then in step (c) of claim 24, one "determin[es] the sequence of the double stranded nucleic acid sample and the position of the at least one modified base in the sequence" by comparing the sequences of the forward and reverse strands. *Id.* col. 47 ll. 41–49.

The '630 patent describes the bisulfite conversion of a CPLM as one embodiment of the methods for detecting modified bases, *id.* col. 23 ll. 44–65, col. 26, ll. 10–23, and illustrates in Figure 5B, which is shown below, a bisulfite-treated CPLM with matched ^{m}C-G and mismatched G-U base pairs, *id.* col. 6 ll. 16–23.



Id. fig.5B.

Additionally, claim 23 of the '630 patent requires that the forward and reverse strands of the double-stranded nucleic acid be locked together by two nucleic acid inserts of known sequences to form the CPLM. *See id.* fig.3A & 3B (depicting a CPLM made from the forward and reverse strands 11 and 12 and two inserts 13 and 14). Because sequencing data from a given experiment may not be 100% accurate, claim 23 provides that the CPLM is sequenced multiple times; that each set of the sequence data of the *inserts* is scored by comparing the measured sequence with the known sequence, *id.* col. 47 ll. 15–18; and that a given set of the sequence data of the *forward or reverse strand* is then accepted or rejected based on "the scores of one or both of the sequences of the inserts immediately upstream and downstream of the sample sequences," *id.* col. 47 ll. 19–25.

Claim 23 depends from claim 1; both claims are reproduced below.

> 1. A method of determining a sequence of a double-stranded nucleic acid sample and a posi-

tion of at least one modified base in the sequence, comprising:

a. locking the forward and reverse strands together to form a circular pair-locked molecule;

b. obtaining sequence data of the circular pair-locked molecule via single molecule sequencing, wherein the sequence data comprises sequences of the forward and reverse strands of the circular pair-locked molecule;

c. determining the sequence of the double-stranded nucleic acid sample by comparing the sequences of the forward and reverse strands of the circular pair-locked molecule;

d. altering the base-pairing specificity of bases of a specific type in the circular pair-locked molecule to produce an altered circular pair-locked molecule;

e. obtaining the sequence data of the altered circular pair-locked molecule wherein the sequence data comprises sequences of the altered forward and reverse strands; and

f. determining the positions of modified bases in the sequence of the double-stranded nucleic acid sample by comparing the sequences of the altered forward and reverse strands.

23. The method of claim 1, wherein:

the forward and reverse strands of the circular pair-locked molecule are locked together by nucleic acid inserts;

the sequence data obtained in step (b) comprise at least two copies of the sequence of the circular pair-locked molecule, each copy comprising sequences of first and second insert-sample units;

the sequences of the first and second insert-sample units comprise insert sequences, which may be identical or non-identical, and oppositely oriented repeats of the sequence of the nucleic acid sample; and

the method further comprises:

g. calculating scores of the sequences of at least four inserts contained in the sequence data by comparing the sequences of the at least four inserts to the known sequences of the inserts;

h. *accepting or rejecting at least four of the repeats of the sequence of the nucleic acid sample contained in the sequence data according to the scores of one or both of the sequences of the inserts immediately upstream and downstream of the sample sequences*, subject to the condition that at least one sample sequence in each orientation is accepted;

i. compiling an accepted sequence set comprising the at least one sample sequence in each orientation accepted in step (g); and

j. determining the sequence of the nucleic acid sample using the accepted sequence set.

Id. col. 45 ll. 24–47, col. 47 ll. 3–30 (emphasis added).

Lastly, claims 27 and 28 of the '630 patent require the use of a "nucleotide analog that discriminates between a

base and its modified form" in sequencing. *Id.* col. 48 ll. 28–33, 45–50. The '630 patent describes such a compound as a "discriminating analog" that "pairs preferentially with one but not the other of the base and its modified form." *Id.* col. 24 ll. 15–19. The '630 patent also provides examples of "discriminating analogs" that were known in the art. *Id.* col. 24 l. 42–col. 25 l. 24 (citing U.S. Patent 7,399,614). Those examples are base-linked analogs, meaning that they have bulky groups chemically linked to the base moiety, allowing them to pair preferentially with a base or its modified form during sequencing. Claim 27 is representative of those two claims and reads as follows:

> 27. A method of determining a sequence of a double-stranded nucleic acid sample and a position of at least one modified base in the sequence, comprising:
>
> a. locking the forward and reverse strands together to form a circular pair-locked molecule;
>
> b. obtaining sequence data of the circular pair-locked molecule via single molecule sequencing, wherein the sequence data comprises sequences of the forward and reverse strands of the circular pair-locked molecule;
>
> c. determining the sequence of the double-stranded nucleic acid sample by comparing the sequences of the forward and reverse strands of the circular pair-locked molecule;
>
> d. obtaining sequencing data of the circular pair-locked molecule via single molecule sequencing, *wherein at least one nucleotide analog that discriminates between a base and its modified form is used to obtain se-*

quence data comprising at least one position wherein the at least one differentially labeled nucleotide analog was incorporated; and

e. determining the positions of modified bases in the sequence of the double-stranded nucleic acid sample by comparing the sequences of the forward and reverse strands.

Id. col. 48 ll. 15–37 (emphasis added).

III

PacBio owns by assignment U.S. Patent Application 13/633,673 ("the '673 application") and U.S. Patent Application 13/930,178 ("the '178 application"). PacBio copied the '630 patent claims into its '673 application to provoke an interference with ITRI.[2] In October 2013, the Board declared Interference No. 105,970 between PacBio's '673 application and ITRI's '630 patent. Three months later, PacBio's '178 application was added to the interference.

The interference involves a sole count corresponding to all twenty-eight claims of ITRI's '630 patent and all pending claims of PacBio's '673 and '178 applications. The Count is identical to claim 24 of the '630 patent.

When declaring the interference, the Board accorded PacBio the benefit of the '551 application, filed on December 11, 2008, and accorded ITRI the benefit of an applica-

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[2] The parties do not dispute that ITRI's '630 patent and PacBio's '673 and '178 applications all have effective filing dates before the enactment of the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284 (2011). The pre-AIA versions of 35 U.S.C. §§ 102, 103, and 112 therefore apply in this appeal. *See* Pub. L. No. 112-29, § 3(n)(1), 125 Stat. at 293.

tion filed on April 7, 2009. Based on those filing dates, the Board designated PacBio as the senior party.

The parties then filed preliminary motions, including ITRI's motion seeking to rescind the benefit of PacBio's '551 application ("rescind motion") and PacBio's motion alleging that all claims of ITRI's '630 patent would have been obvious in view of the prior art ("obviousness motion"). The prior art asserted by PacBio against ITRI's '630 patent included: (1) U.S. Patent 8,153,375 ("the '375 patent"), assigned to PacBio; (2) PacBio's Cold Spring Harbor Personal Genomes Meeting Presentation, dated October 12, 2008 ("the Personal Genomes presentation"); (3) Laird *et al.*, *Hairpin-bisulfite PCR: Assessing epigenetic methylation patterns on complementary strands of individual DNA molecules*, 101 Proc. Nat'l Acad. Sci. 204 (2004) ("Laird"); (4) Matsumura *et al.*, *Photochemical transition of 5-methylcytosine to thymine by DNA photoligation*, 51 Nucleic Acids Symp. Series 233 (2007) ("Matsumura"); and (5) U.S. Patent 7,399,614 ("the '614 patent").

In a written decision on September 3, 2014, the Board granted PacBio's obviousness motion and denied ITRI's rescind motion. In granting PacBio's obviousness motion, the Board concluded that all claims of ITRI's '630 patent would have been obvious in view of the '375 patent, Laird, and Matsumura. *Board Decision*, 2014 WL 4381078, at *20. Although the Board cited Matsumura, its obviousness analysis did not rely on any specific teachings of Matsumura. The Board also did not rely on the '614 patent cited by PacBio. Moreover, the Board did not consider the Personal Genomes presentation, after finding that it was not prior art under 35 U.S.C. § 102(b). *Id.* at *13 n.27. Thus, the Board relied only on the '375 patent and Laird as prior art in its obviousness analysis.

First, as to claim 24, which the parties regarded as representative of most of the claims of the '630 patent, the

Board noted that ITRI did not dispute that the '375 patent taught steps (a) and (b) of claim 24. The Board then found that Laird taught step (c), and thus concluded that claim 24 would have been obvious in view of the '375 patent and Laird. *Id.* at *20–21. Second, the Board rejected ITRI's argument that the prior art did not teach step (h) of claim 23; instead, the Board found that the '375 patent and Laird taught that limitation. *Id.* at *22. Last, as to claims 27 and 28, which require a nucleotide analog that discriminates between a base and its modified form, the Board concluded that those claims would have been obvious because "Laird teaches such a method [of] discriminating between methylated and non-methylated cytosines." *Id.* at *22–23.

The Board accordingly found all claims of the '630 patent to be unpatentable as obvious because "[t]he combined cited prior art references teach or suggest all of the limitations of the claims of the '630 patent" and "a person of ordinary skill in the art would be motivated to combine the references to increase the accuracy of the invention, particularly with respect to discriminating between methylated and demethylated cytosine bases." *Id.* at *23. The Board did not opine on whether the references cited by PacBio would be prior art to PacBio's own claims, thus rendering them similarly unpatentable as obvious, even though the parties disputed that issue. J.A. 269–70, 346, 421, 750–52.

In denying ITRI's rescind motion, the Board found that PacBio was entitled to the benefit of the filing date of the '551 application because that application provided an adequate written description of an embodiment of the Count. *Board Decision*, 2014 WL 4381078, at *28–31. In particular, the Board found that the '551 application teaches step (c) of the Count, in part, because the application explicitly states that "'sequence reads from the sense or 'forward' strand can be compared to sequence reads from the antisense or 'reverse' strand for the same nucleic

acid template to further validate the existence of one or more modified bases in the template nucleic acid.'" *Id.* at *28–29 (quoting '551 application ¶ 17).

The Board entered judgment against ITRI. *Id.* at *1. ITRI then appealed to this court. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A). *See* Leahy-Smith America Invents Act Technical Corrections, Pub. L. No. 112-274, § 1(k)(3), 126 Stat. 2456, 2458 (2013).

DISCUSSION

I. OBVIOUSNESS OF ITRI'S PATENT CLAIMS

We review the Board's legal determinations *de novo*, *In re Elsner*, 381 F.3d 1125, 1127 (Fed. Cir. 2004), and the Board's factual findings underlying those determinations for substantial evidence, *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). A finding is supported by substantial evidence if a reasonable mind might accept the evidence to support the finding. *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938).

Obviousness is a question of law based on underlying factual findings, *In re Baxter*, 678 F.3d 1357, 1361 (Fed. Cir. 2012), including what a reference teaches, *In re Beattie*, 974 F.2d 1309, 1311 (Fed. Cir. 1992), the existence of a reason to combine references, *In re Hyon*, 679 F.3d 1363, 1365–66 (Fed. Cir. 2012), and whether the prior art teaches away from the claimed invention, *In re Mouttet*, 686 F.3d 1322, 1330 (Fed. Cir. 2012).

A. Claims 1–22 and 24–26

ITRI argues that the Board erred in finding that Laird teaches determining the position of a modified base by comparing the sequences of the forward and reverse

strands as required by step (c) of claim 24.[3] According to ITRI, researchers in Laird used conventional methods to determine the positions of modified bases, by comparing the sequences of bisulfite-treated and untreated versions of the same strand, not the forward and reverse strands of the same molecule as claimed by ITRI. ITRI asserts that the Board improperly engaged in hindsight analysis by speculating that a skilled artisan would have understood that mismatches in the sequences of the forward and reverse strands would indicate modified base positions. According to ITRI, only the '630 patent, not Laird or any other prior art, teaches using *mismatches* to detect modified bases.

PacBio responds that the claims do not require using *mismatches* to detect modified bases because a preferred embodiment of the '630 patent, involving bisulfite conversion of C (but not ^{m}C) to U, uses *matches* of ^{m}C to G to detect the ^{m}C positions. Appellee's Br. 29–33 (citing '630 patent col. 26 ll. 10–22). PacBio alternatively argues that, even if the use of mismatches were required, the claims would still have been obvious because substantial evidence supports the Board's finding that Laird teaches that limitation. PacBio additionally argues that a person of skill in the art would have been motivated to combine the prior art to practice the claimed method and achieve a predictable result, that one would have had a reasonable expectation of success in doing so, and that there is no evidence of objective indicia of nonobviousness.

We agree with PacBio that the Board did not err in its obviousness determination as to claims 1–22 and 24–26

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[3] ITRI relies only on limitations in claim 24 to challenge the obviousness determination as to claims 1–22 and 24–26. *See* Appellant's Br. 29. Those claims therefore stand or fall together with claim 24. *In re Kaslow*, 707 F.2d 1366, 1376 (Fed. Cir. 1983).

because Laird suggests using mismatches in the sequences of the forward and reverse strands to determine modified base positions. ITRI does not dispute that the '375 patent discloses steps (a) and (b) of claim 24. Nor does ITRI challenge the Board's finding of a motivation to combine the '375 patent and Laird. The only question is then whether substantial evidence supports the Board's finding that Laird teaches step (c) of claim 24, and we conclude that it does.

As an initial matter, the record shows that the Board did not formally construe the claims. In the background section of the Board's written decision, it informally interpreted step (c) of claim 24, or the Count, as requiring the use of mismatches in determining modified base positions, which is what ITRI proposed. *Board Decision*, 2014 WL 4381078, at *3. Applying that claim interpretation, the Board decided the obviousness motion and the rescind motion against ITRI. *Id.* at *21, *30.

The Board's claim interpretation is consistent with the claim language and specification of the '630 patent. Contrary to PacBio's arguments, that interpretation does not exclude the bisulfite method disclosed in the '630 patent, in which bisulfite converts C, but not ^{m}C, to U in a CPLM. When comparing the sequences of the forward and reverse strands of such a bisulfite-treated CPLM, one would find both *matched* ^{m}C-G pairs and *mismatched* U-G pairs. The bisulfite method does use mismatched U-G pairs in distinguishing C from ^{m}C and in determining the positions of modified bases, which may be either U or ^{m}C. The parties do not otherwise allege error in the Board's claim interpretation. Accordingly, on this record, we conclude that the Board did not err in interpreting step (c)

of claim 24, or the Count, as requiring the use of mismatches in determining modified base positions.[4]

Although we agree with ITRI on the proper interpretation of step (c) of claim 24, we nevertheless conclude that substantial evidence supports the Board's finding that the disclosure of Laird would have suggested that claim limitation to a person of ordinary skill in the art. Laird teaches "hairpin-bisulfite PCR." J.A. 722. It explains that "[b]isulfite conversion . . . provides information on the methylation state of individual cytosines by converting cytosine (but not 5-methylcytosine) to uracil . . . ." J.A. 723. Thus, Laird teaches that modified bases can be detected through the use of bisulfite treatment.

As disclosed in Laird, a double-stranded DNA was ligated on one end with a hairpin linker, and the covalently linked forward and reverse strands were treated with bisulfite and then sequenced. *Id.* According to Laird, "[f]or purposes of *analysis* and presentation, the output sequence was folded, using word-processing software, into a hairpin conformation so that *both strands align*." *Id.* (emphases added). Laird depicts in Figure 2 several pairs of forward and reverse strands side-by-side that have mismatches in the sequences of the forward and reverse strands as a result of the bisulfite treatment. J.A. 725. Laird explains that "[w]ith hairpin-bisulfite PCR, we can assess the methylation status on the *bottom strand* of each hypermethylated allele for which we have *top-strand* data," and that "we can distinguish between symmetrical and asymmetrical patterns of methylation for each of the

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[4] PacBio filed a motion in this court to strike certain arguments made in ITRI's reply brief, relating to the prosecution history of the '630 patent, as improperly raised for the first time on appeal. Because our decision does not turn on those arguments, we dismiss PacBio's motion as moot.

CpG/CpG dyads." J.A. 724 (emphases added). Moreover, Figure 2D shows several asymmetrical hemimethylated CpG/CpG dyads, in which one strand of the DNA has a ^{m}C and the other has a C. J.A. 725.

Substantial evidence therefore supports the Board's finding that "Laird teaches that methylated and unmethylated [CpG] dyads in a bisulfite-treated DNA sequence can be identified by the matching or mismatching of cytosines in the forward and reverse strand sequence data," *Board Decision*, 2014 WL 4381078, at *20, and that "Laird explicitly teaches looking for guanine-thymine mismatches as evidence of non-methylated cytosine in a forward or reverse strand locus," *id.* at *21. We therefore conclude that the Board did not err in finding that Laird would have suggested to a person of ordinary skill in the art that mismatched base pairs in the sequences of the forward and reverse strands may be used to determine the positions of modified bases in double-stranded DNA.

Accordingly, we affirm the Board's determination that claims 1–22 and 24–26 would have been obvious over the '375 patent and Laird.

B. Claim 23

ITRI argues that the Board additionally erred in finding claim 23 obvious because the Board failed to find that the prior art taught step (h) of claim 23, which requires accepting or rejecting a given data set of a DNA *sample sequence* based on the score calculated for an *insert sequence* immediately upstream or downstream from the sample sequence. ITRI contends that the Board failed to otherwise point to any record evidence to support its finding that the prior art taught step (h).

PacBio responds that step (h) of claim 23 would have been obvious in view of the '375 patent. PacBio argues that the level of skill in the art was high and that, even if the '375 patent does not precisely teach step (h), a skilled

artisan would have nonetheless found the differences between the claimed invention and the '375 patent to be insubstantial and therefore obvious.

We agree with ITRI that the Board did not sufficiently address whether the prior art teaches step (h) of claim 23 or otherwise would have rendered that limitation obvious. It is undisputed that claim 23 requires that, when analyzing multiple reads of the CPLM sequence, one accepts or rejects a given data set of the forward or reverse strand sequence based on the score of a *different* sequence—the insert sequence upstream or downstream from the forward or reverse strand sequence. But the Board's cursory obviousness analysis with respect to claim 23 lacks any indication that the Board considered that claim limitation in view of the prior art. The Board's analysis seems to mainly focus on using multiple reads of one position in the sequence to determine the consensus sequence of that *same* position. *Board Decision*, 2014 WL 4381078, at *22.

It may be true that, in view of the cited prior art and the level of ordinary skill in the relevant art, the differences between step (h) of claim 23 and the prior art would have been insubstantial. But the scope and content of the prior art and the differences between the prior art and the claimed invention are issues of fact to be decided by the Board, not this court. *Cooper v. Ford Motor Co.*, 748 F.2d 677, 679 (Fed. Cir. 1984). The Board did not make sufficient factual findings in its written decision or otherwise point to evidence that a skilled artisan would have accepted or rejected a sample sequence based on the score of a *different* insert sequence that is upstream or downstream from the sample sequence. We therefore vacate the obviousness determination as to claim 23 and remand for further proceedings at the Board.

C. Claims 27 and 28

ITRI argues that the Board erred in finding claims 27 and 28 obvious because neither the '375 patent nor Laird,

which the Board relied on, discloses the use of a discriminating nucleotide analog as required by the claims. ITRI also contends that the Board provided no explanation for why the missing claim limitation would nonetheless have been obvious. ITRI also argues that the Board improperly disregarded evidence that the Personal Genomes presentation taught away from using base-linked analogs, which include discriminating nucleotide analogs, and thus would have discouraged a skilled artisan from combining the '375 patent with a discriminating nucleotide analog.

PacBio responds that its obviousness arguments before the Board were based on the combination of the '375 patent with the '614 patent, not Laird, and that ITRI does not dispute that the '614 patent teaches discriminating nucleotide analogs. PacBio thus argues that, to the extent the Board erred in finding that Laird teaches a discriminating nucleotide analog, that error is harmless because claims 27 and 28 would have been obvious in view of the '375 and '614 patents. PacBio also argues that the Personal Genomes presentation does not teach away from the use of a discriminating nucleotide analog or the use of a base-linked nucleotide analog in general.

We agree with ITRI that the Board erred in concluding that claims 27 and 28 would have been obvious over the combination of the '375 patent and Laird. The claims require the use of a "nucleotide analog that discriminates between a base and its modified form." The '630 patent explains that a "discriminating analog . . . pairs preferentially with one but not the other of the base and its modified form." '630 patent col. 24 ll. 15–19. The Board did not find, and PacBio does not contend, that either the '375 patent or Laird teaches such a discriminating nucleotide analog. The Board only found that Laird taught "discriminating between methylated and non-methylated cytosines." *Board Decision*, 2014 WL 4381078, at *23. But Laird's method uses bisulfite to convert C to U and then distinguishes C from ^{m}C for the fact that U pairs with A

and ^{m}C pairs with G. The Board did not otherwise indicate why the "discriminating nucleotide analog" limitation would have been obvious in view of the record evidence.

Although the '614 patent, cited by PacBio, does disclose discriminating nucleotide analogs, the parties dispute whether the Personal Genomes presentation teaches away from combining the '375 and '614 patents. ITRI argued to the Board that the Personal Genomes presentation taught away from using base-linked analogs in the sequencing methods described in the '375 patent. J.A. 344. But the Board did not consider the disclosure of the Personal Genomes presentation, after finding that it was not prior art under 35 U.S.C. § 102(b). *Board Decision*, 2014 WL 4381078, at *13 n.27. The Board did not consider whether the Personal Genomes presentation would qualify as prior art under other subsections of § 102, such as § 102(a).

Whether the prior art teaches away from the claimed invention is a question of fact. *Mouttet*, 686 F.3d at 1330. The Board did not consider some of the cited prior art, including the Personal Genomes presentation, and it did not properly determine whether a skilled artisan would have pursued the method of claims 27 and 28, which uses a discriminating nucleotide analog. We therefore vacate the obviousness determination as to claims 27 and 28 and remand for further proceedings at the Board.

II. CROSS-APPLICABILITY OF THE PRIOR ART

Section 41.207(c) of Title 37 of the Code of Federal Regulations provides:

> When a motion for judgment of unpatentability against an opponent's claim on the basis of prior art is granted, each of the movant's claims corresponding to the same count as the opponent's claim will be presumed to be unpatentable in view

> of the same prior art unless the movant in its motion rebuts this presumption.

37 C.F.R. § 41.207(c) (cross-applicability of prior art).

Before the Board, PacBio asserted the '375 patent, which it owns, as prior art under 35 U.S.C. § 102(e), and it sought to establish common ownership of the '375 patent and its '673 and '178 applications under § 103(c), in order to disqualify the '375 patent as prior art against itself. When the Board granted PacBio's obviousness motion, invalidating all of ITRI's claims, it did not opine on the patentability of PacBio's claims or otherwise indicate whether PacBio has overcome the presumption of cross-applicability of the cited prior art.

ITRI argues that the Board erred by failing to hold PacBio's claims unpatentable pursuant to 37 C.F.R. § 41.207(c). ITRI also argues that PacBio failed to rebut the presumption of cross-applicability, and that the Board incorrectly analyzed common ownership under 35 U.S.C. § 103(c). PacBio responds that it has rebutted any presumption of cross-applicability by explaining to the Board that the '375 patent does not preclude patentability of its claims under § 103(c) and by submitting a declaration with its reply. PacBio also argues that the Board properly exercised its discretion not to apply the presumption.

On this record, it is unclear whether the Board implicitly determined that PacBio has overcome the presumption of cross-applicability or whether the Board decided not to apply the prior art to PacBio's claims for some other reason. Because we affirm the obviousness determination as to claims 1–22 and 24–26 of ITRI's '630 patent and remand the case for further determinations as to claims 23, 27, and 28 of that patent, the Board will have another opportunity to address the cross-applicability issue.

The record does show, however, that the Board might have misunderstood what was required to disqualify prior

art under 35 U.S.C. § 103(c). In an August 2014 decision denying ITRI's motion to strike PacBio's reply brief and accompanying declaration, the Board reasoned:

> It is therefore evident that, regardless of *who* the inventors of the '375 patent and '673 and '178 applications were, the Moore Declaration provides evidence in support of PacBio's contention that the patent and applications *had been assigned to*, *and were owned by*, PacBio. That PacBio is the assignee of the '375 patent and '673 and '178 applications, *no matter who the inventors were*, is not disputed by the parties. To that extent, *viz.*, the issue of common ownership, the Board will consider the evidentiary weight of the Moore Declaration in support of PacBio's arguments. With respect to inventorship, the Board will defer that issue to the priority phase of the interference . . . .

Indus. Tech. Research Inst. v. Pac. Biosciences of Cal., Inc., Interference No. 105,970, Paper 166, at *9 (P.T.A.B. Aug. 11, 2014) (first emphasis in original) (second and third emphases added) (J.A. 480).

It appears that the Board might have misapplied § 103(c) by reasoning that the assessment of common ownership may be based on evidence of common ownership by assignment, even if the assignment occurred *after* the application filing date. 35 U.S.C. § 103(c) provides that § 102(e) prior art does not preclude patentability if "the subject matter [of the prior art] and the claimed invention were, *at the time the claimed invention was made*, owned by the same person or subject to an obligation of assignment to the same person" (emphasis added). Accordingly, evidence of common ownership by assignment after the application filing date does not establish common ownership or an obligation to assign ownership *at the time of the invention*.

We therefore remand for a determination of the cross-applicability of the cited prior art to PacBio's claims and, if necessary, a proper analysis of common ownership of the '375 patent and the '673 and '178 applications.

III. WRITTEN DESCRIPTION IN THE '551 APPLICATION

Sufficiency of written description is a question of fact, which we review for substantial evidence. *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). Claims must be sufficiently supported by the written description of a patent, such that the disclosure "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* To receive the benefit of an earlier application in an interference, the application must contain an adequate written description of at least one embodiment of the count. *Tobinick v. Olmarker*, 753 F.3d 1220, 1227 (Fed. Cir. 2014).

ITRI argues that the Board erred in designating PacBio the senior party because the '551 application lacks a written description of the Count, in particular, any express or inherent disclosure of using mismatched base pairs to determine modified base positions. According to ITRI, paragraph 17 of the '551 application, including its reference to comparing the forward and reverse strands, merely describes using base-pair matches, not mismatches, to confirm the reliability of sequencing data. ITRI also asserts that the '551 application disclaims the bisulfite embodiment of the Count because the '551 application states that its methods do not "rel[y] on the similarity of uracil to thymine." Appellant's Br. 41 (quoting '551 application ¶ 23). ITRI explains that the Count relies on the similarity of U and T, because, when U is the modified base after bisulfite treatment, the claimed method relies on the fact that both U and T pair with A in sequencing.

PacBio responds that the Board correctly found that the '551 application discloses an embodiment of the Count

because it expressly discloses (1) a CPLM DNA sequencing template, (2) the use of bisulfite treatment, and (3) the comparison of forward and reverse strands of the CPLM to identify modified bases. PacBio argues that the Count does not require using *mismatches* to determine the positions of modified bases. PacBio also argues in the alternative that, even if the Count did require the use of mismatches, the Board's factual finding of adequate written description is supported by substantial evidence, which includes the '551 application's express disclosures and the detailed testimony of PacBio's expert witness explaining the disclosures of the '551 application.

As indicated *supra*, we conclude that the Board properly interpreted the Count as requiring the use of mismatched base pairs in detecting modified base positions. Under that construction, we conclude that substantial evidence supports the Board's finding that the '551 application adequately describes an embodiment of the Count. The '551 application describes methods of detecting modified bases. The application discloses a CPLM template, as well as the use of bisulfite to convert C, but not ^{m}C, to U. J.A. 918–20. The application defines "modified bases" as including "methylated bases" and "bisulfite-converted bases." J.A. 919.

Importantly, the application states in paragraph 17 that "sequence reads from the sense or 'forward' strand can be *compared* to sequence reads from the antisense or 'reverse' strand for the same nucleic acid template to further *validate the existence of one or more modified bases* in the template nucleic acid." J.A. 918 (emphases added). That is an explicit reference to comparing the forward and reverse strands and using base-pair matches and mismatches to detect modified bases. Although other portions of the '551 application describe prior-art consensus sequencing technique, those disclosures do not alter the explicit reference to "compar[ing]" the forward and reverse strand sequences to determine "the existence of

one or more modified bases." Likewise, we find ITRI's argument that paragraph 23 of the application disclaims the bisulfite embodiment of the Count to be unpersuasive.

We therefore affirm the Board's finding that the '551 application provides an adequate written description of at least one embodiment of the Count.

CONCLUSION

We have considered the parties' remaining arguments, but find them unpersuasive. For the foregoing reasons, we affirm the Board's decision that claims 1–22 and 24–26 of ITRI's '630 patent would have been obvious over the cited references and that PacBio's '551 application contains an adequate written description of an embodiment of the Count. Additionally, we vacate the Board's obviousness judgment as to claims 23, 27, and 28 of the '630 patent and remand for a further determination of the patentability of those claims and for the Board to address the cross-applicability of the cited prior art to PacBio's involved claims.

AFFIRMED IN PART, VACATED IN PART, AND REMANDED

COSTS

No costs.